REMARKS/ARGUMENTS

Amendment to the Specification

The specification has been amended to add the sentence: "In another embodiment of the present invention, the dosage range is from about 0.5 to about 10 mg." This amendment is supported by originally filed claim 35, which contained this limitation. Therefore, no new matter is introduced.

Claim Status

Claims 72-76 and 87-96 are pending in the instant application. Claims 77-86 are held withdrawn, as being drawn to a non-elected species. Claims 1-71 were previously canceled without prejudice to their presentation in one or more continuing applications directed to the subject matter thereof. Claims 87-90 and 92-95 are presently canceled without prejudice.

Claim Objections

Claims 75 and 76 were objected to because each claim recited the same compound with different names. Claim 75 has been amended to include the parenthetical equivalent name of eplerenone for the compound Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ-lactone, methyl ester, (7a,11a,17a)-. Since the specification shows this structure, and teaches that Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-, γ-lactone, methyl ester, (7a,11a,17a)- is eplerenone, no new matter is introduced.

Claim 75 was objected to because it recited "(γ-lactone" at line 3. Claim 75 has been amended to remove the parenthesis, as well as similar parentheses at lines 8, 14, 20, 21 and 28. These parentheses do not appear in the description of each compound recited in claim 75, in the specification at page 19, lines 5-15 (second paragraph) through page 22, lines 1-15, and therefore no new matter is introduced.

Claim Amendments

Claim 72 has been amended to include the limitation of an "effective amount of an epoxy-steroidal aldosterone receptor antagonist compound that produces no substantial diuretic or anti-hypertensive effect in the subject."

Support for this amendment may be found, for example, in the specification page 10, lines 13 through 15, and therefore, no new matter is introduced.

Claim 75 has been amended to excise a typographic error, removing parentheses before "γ-lactone," as described above.

Claim 76 has been amended to add the parenthetical designation of "eplerenone" after "Pregn-4-ene-7,21-dicarboxylic acid, 9,11-epoxy-17-hydroxy-3-oxo-,(γ-lactone, methyl ester, (7α 11α,17α)-." Support for this amendment may be found in the specification, for example, at page 19 (TABLE I) lines 5-10 and page 23, lines 1-2.

Claim rejections Under 35 U.S.C. § 102

Claims 72-76 and 87-96 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Grob et al., U.S. Patent 4,559,332.

Claims 72-76 and 87-96 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Thosar et al., U.S. Patent 6,410,054.

For purposes of this amendment, amended claim 72 will be discussed.

The Claims, as Amended, are not Anticipated

A claim is anticipated if a single prior art reference discloses each and every limitation of the claimed invention. Lewmar Marine, Inc. v. Barient, Inc., 827 F.2d 744, 747 (Fed. Cir. 1987). Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference. Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268 (Fed. Cir. 1991). Further, Anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure. In re Donohue, 766 F.2d 531, 533 (Fed. Cir. 1985). 226 U.S.P.Q. (BNA) 619.

Without acquiescing to the rejections under 35 U.S.C. § 102 made in the Office Action dated February 23, 2004, Applicants assert that the claims, as amended, contain limitations that are not present in either Grob et al, or Thosar et al.

Neither Grob et al. nor Thosar et al. teach or suggest a dose of epoxy-steroidal aldosterone antagonist in an amount "that produces no substantial diuretic or anti-hypertensive effect in the subject," as presently amended claim 72 now requires. All of the pending claims depend from claim 72, and therefore, none of the pending claims are anticipated by either Grob et al. or Thosar et al.

Please note that Grob et al. discloses dosage units of 5-150 mg. Only when combined with a second, diuretic compound. Grab states at Column 15, lines 10-17:

> As a special form of these pharmaceutical compositions and medicaments according to the invention there come into consideration also those which contain, **in addition to** the aldosterone-antagonistic compound of the formula I (including salts) according to the invention, **which is referred to as component A** in this context, **also a diuretic component B which is non-specific with regard to electrolytes**. (emphasis added)

Grob et al, goes on to state, at Column 15, lines 63-68 to Column 16, lines 1-16:

> For example, **such combination preparations** contain, per dosage unit, from 5 to 150 mg, especially from 10 to 50 mg, of **a compound of the formula I** or a salt thereof **as component A** and, as component B, for example from 10 to 100 mg, especially from 25 to 50 mg, of 2-chloro-5- [3- hydroxy-1-oxo-isoindolyl-(3)]-benzenesulphonamide or 4-(2- methylenebutyryl)-2,3-dichlorophenoxyacetic acid, from 5 to 50 mg, especially from 12 to 25 mg, of 6-chloro-7-sulphamyl-3,4-dihydro-1,2,4- benzothiadiazine 1,1-dioxide or 2-chloro-4-furfurylamino-5-carboxybenzenesulphonamide, from 2 to 20 mg, especially from 5 to 10 mg, of 2-phenoxy-3- 3-(1-pyrrolyl)-propyl!-5-carboxybenzenesulphonamide, from 0.1 to 1.0 mg, especially from 0.25 to 0.5 mg, of 3- cyclopentylmethyl-6-chloro-7-sulphamoyl-3,4-dihydro-1,2,4- benzothiadiazine 1,1-dioxide or 2-phenoxy-3-butylamino-5- carboxybenzenesulphonamide, from 100 to 400 mg, especially 200 mg, of 4- thenoyl-2,3-dichlorophenoxyacetic acid and from 5 to 25 mg, especially 10 mg, of racemic (1-oxo-2-methyl-2-phenyl-6,7-dichloro-5-indanyloxy)- acetic acid, or half the amount of the laevo-form of this acid. (emphasis added).

Thus, it can be seen that Grob et al. does not fairly enable the use of an epoxy-steroidal compound in an amount "that produces no substantial diuretic or anti-hypertensive effect in the subject," as presently amended claim 72 now requires. Also note that claims 91

and 96, which contain the limitation of administration of from about 0.5 to about 10 mg, further carry the limitation of administering an epoxy-steroidal compound in an amount "that produces no substantial diuretic or anti-hypertensive effect in the subject," since both claims 91 and 92 depend from Claim 72.

Finally, neither Grob et al. nor Thosar et al. are enabling for a method that includes administering an amount of an epoxysteroidal aldosterone antagonist to a subject in an amount that produces substantially no diuretic or anti-hypertensive effect. While both references describe a broad range of dosages, "An invitation to investigate is not an inherent disclosure." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 2004 U.S. App. LEXIS 11248, *31, Docket 03-1120, Fed. Cir. 2004). Since neither Grob et al., nor Thosar et al. describe the limitations present in the claims, as amended, the claims are not anticipated.

Claim rejections Under 35 U.S.C. § 103

Claims 72-76 and 87-96 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Grob et al. in view of MacLaughlan et al. (WO 96/24358); and over Thosar et al.

The Claims, as Amended, are not Obvious

None of the references of record teach or suggest the limitation of administering an amount of an epoxysteroidal aldosterone antagonist to a subject in an amount that produces substantially no diuretic or anti-hypertensive effect, as the presently amended claims require. MacLaughlan et al. teaches administering spironolactone at a low dose to reduce or avoid side effects of spironolactone. (See WO 96/24358, page 1, lines 1-13.)

Grob et al. states, at Column 3, lines 48-62:

> 20-Spiroxane derivatives having an aldosterone-antagonistic action are known, cf., for example, Fieser and Fieser: Steroids; page 708 (Reinhold Publ. Corp., New York, 1959) and British Patent Specification No. 1,041,534; also known are analogously active 17β- □ydroxyl-21-carboxylic acids and their salts, cf., for example, U.S. Pat. No. 3,849,404. Compounds of this kind that have hitherto been used in therapy, however, have a considerable disadvantage in that they always possess a certain sexual-specific activity which has troublesome consequences sooner or later in the customary long-term therapy. Especially undesirable are the

> troublesome effects that can be attributed to the anti-androgenic activity of the known anti-aldosterone preparations.

Grob further states, at Column 3 lines 63-68 to Column 4, line 1:

> It has now been found that the above-characterised 9α,11α-epoxy compounds of the formula I surprisingly exhibit these undesirable side-effects to a substantially lesser degree although they completely retain the favourable anti-aldosterone action of compounds that have an analogous structure but that are not substituted in the 9, 11-position.

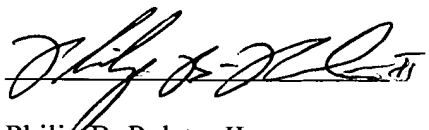
Therefore, one skilled in the art would not be motivated to combine the teachings of Grob et al. with the teachings of MacLaughlan et al., since the lower dosage taught in MacLaughlan et al. would apparently not be necessary when administering the compounds of Grob et al.

Further, MacLaughlan et al. teaches that there are several underlying causes of Heart Failure, such as hypertension or cardiomyopathy (See page 1, lines 17-21). Applicants believe that administering an epoxy-steroidal aldosterone antagonist in an amount that produces substantially no diuretic or anti-hypertensive effect would not be made obvious considering this teaching.

Thosar et al. does not teach or suggest administering an epoxy-steroidal aldosterone antagonist in an amount that produces substantially no diuretic or anti-hypertensive effect, nor does it teach treatment or prevention of myocardial infarction. Therefore, it is believed that Thosar et al., alone or in combination with any other reference, does not render the instant claims obvious.

If a telephonic interview with Applicant's representative would aid in the prosecution of this application, the Examiner is cordially invited to contact Applicant's representative at the below listed number.

Respectfully submitted,



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